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EXAMINER	
SKOWRONEK, KARLHEINZ R	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/734,023	VANET ET AL.	
	Examiner	Art Unit	
	KARLHEINZ R. SKOWRONEK	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *11-19,21-27,30 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,20,28,29,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1-33 are pending.

Claims 11-19, 21-27, and 30-31 are withdrawn as being directed to a non-elected invention as indicated in the response filed June 4 2007 and the restriction requirement of 4 May 2007.

Claims 32-33 are new.

Claims 1-10, 20, 28-29, and 32-33 have been examined.

Claims 1-10, 20, 28-29, and 32-33 are rejected.

Interview Summary

The summary of the interview is accurate.

Claim Objections

The objections to claims 4 and 6 are withdrawn in view of the amendments to the claims.

Claim Rejections - 35 USC § 101

The rejection of claims 1-10, 20, and 28-29 as non-statutory under 35 USC 101 is withdrawn in view of the amendments to the claims.

Claim Rejections - 35 USC § 112

The rejection of claim 1 as indefinite under 35 USC 112 is withdrawn in view of the amendments to the claim.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The following is a new ground of rejection.

Claims 6-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites the limitation "the other cases" in line 7, 13, and 17. There is insufficient antecedent basis for this limitation in the claim.

Claim 6 is unclear with respect to the term "this matrix" in line 8. The metes and bounds of the claim are made indefinite because the claim recites multiple matrices; however line 8 refers to a single matrix in the term "this matrix". The phrase makes it indefinite which matrix "this" refers to.

Claim 6 is unclear with respect to the variable B_2. The metes and bounds of the claim are rendered indefinite because the variable has not been defined. As a result, one does not know how the variable relates to the other elements of the claim. Claims 7 and 8 also rejected because they depend from claim 6, and thus contain the above issues due to said dependence.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

The following rejection presents a new ground of rejection.

Claims 6-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to use the claimed invention one of skill in the art must be able to generate the matrices of mutated and unmutated couples of dimensions MxM. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The description describes the process of generating a matrix of N sequences by M positions or “motifs” in which positions which do not match a reference consensus sequences are set to a value A1 and in other cases is set to A2. Regarding the matrices of mutated and unmutated couples is the following found at [0043]. For the matrix of unmutated couples the specification teaches, “a matrix B of unmutated couples, i.e., of couples which did not mutate

simultaneously, of dimension MxM, the value $B_{i,k} = B_{k,i}$ being equal: to a first value B1 [for example, "O"] when $A_{i,j} = A_{k,j} = A1$ irrespective of the value of j ranging from 0 to N, to a second value B2 [for example "I"] in the other case". For the matrix of mutated couples, the specification teaches, " a matrix C of mutated couples [i.e., of couples that mutate either always, or never simultaneously] of dimension MxM, the value $C_{k,i} = C_{i,k}$ being equal: to a second value C1 [for example, "1"] when $A_{i,j} = A_{k,j}$ irrespective of the value of j ranging from 0 to N, to a first value C2 [for example, "0"] in the other case". The description does not provide detailed guidance for the process of generating the matrices of mutated and unmutated couples of dimensions MxM. The specification does not provide the guidance as to what the "other cases" are in the process of generating the matrices. One is left to guess what the other cases are. The specification also does not disclose how values for B1 and C2 are determined from matrix A. The specification states "$A_{i,j} = A_{k,j}$ =A1 irrespective of the value of j". Thus the specification does not disclose how B1 and C1 are determined from the values in matrix A at positions j and k. The specification fails to disclose how the values for all the independent sequences represented as rows of Matrix A are combined to produce the values of matrices B and C. Both matrices B and C are sequence independent, position dependent matrices. As a result of the lack of guidance in the specification regarding the construction of matrix B and C from Matrix A, one of ordinary skill must guess how to use the information of Matrix A to arrive at matrix B or C.

c) The description provides an example of the matrices produced by the

instant invention. The description does not provide working examples of how the matrices are generated or the relation of the matrices to each other. The examples do not show how the matrices are used to arrive at the result of the method.

d) The nature of the invention, computational biology, is complex.

e) The prior art does not show a matrix B of unmutated couples, i.e., of couples which did not mutate simultaneously, of dimension MxM, the value $B_{i,k} = B_{k,i}$ being equal: to a first value B1 when $A_{i,j} = A_{k,j} = A1$ irrespective of the value of j ranging from 0 to N, to a second value B2 in the other case or a matrix C of mutated couples of dimension MxM, the value $C_{k,i} = C_{i,k}$ being equal: to a second value C1 when $A_{i,j} = A_{k,j}$ irrespective of the value of j ranging from 0 to N, to a first value C2 in the other case, as instantly claimed.

f) The skill of those in the art of computational biology is high.

g) The predictability of the matrices of mutated and unmutated couples of dimensions MxM is unknown in the prior art. Guessing at the other cases introduces unpredictability into the method because one does not know from the claim what the other cases are. Without knowing the other cases the one can not set the values for the cases. As a result one is left to guess the values of the coefficients of R_f and R_e as each is dependent on the other cases.

h) The claims are broad in that they do not set forth what the values for A1, A2, B1, B2, C1, and C2 are or how the values are interrelated. The claims also do not set forth the other cases, leaving to the practitioner to guess at the cases and the values of the coefficients of R_f and R_e, as each is dependent on

the "other cases". Furthermore, the values B1 and C1 are independent of any sequences; this leaves the practitioner to guess how the values B1 and C1 are determined from matrix A. The claims also does not set forth the steps that relate to the interpretation of the matrices such that one can arrive at the result of the method namely the identification a motif whose mutation is linked to another motif mutation.

The skilled practitioner would first turn to the instant description for guidance in using the claimed invention. However, the description lacks clear evidence how to generate the MxM matrices of mutated and unmutated couples. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not discuss how to generate the MxM matrices of mutated and unmutated couples. Finally, said practitioner would turn to trial and error experimentation to determine a relationship between matrix A and Matrices B and C. Such amounts to undue experimentation.

With respect to the declaration of Ms. Sophie Brouillet, filed 06 August 2008, regarding the enablement of the method as claimed in claim 6. The declaration of Ms. Brouillet was previously considered with respect to the rejection of claims 1-10 20 and 28-29 as lacking enablement for identifying mutations in sequences that occurred simultaneously. In the declaration of Ms. Brouillet, the claimed method is outlined in paragraphs 5-10. Ms. Brouillet, in paragraph 5, indicates the working example [0117] to [0130] and [0037] to [0074] provides detailed guidance for performing the method. The paragraph numberings appear to correspond to the US PGPUB document US 20040203028

A1. In Paragraph 6, Ms. Brouillet asserts the steps for performing the method and the rules for constructing the various individual matrices used in the method are readily apparent from inspection of the data values. In paragraphs 7 and 8, Ms. Brouillet describes what is apparent from the specification and in the claims regarding the construction of the NxM matrix A. In paragraph 9 Ms. Brouillet in her explanation of how the B matrix is constructed from the values of the A matrix inserts conditional requirements that are not present in the claim or the description of the method in [0037] to [0074]. Similar to the specification, Ms. Brouillet does not address how all the positions values for each independent sequence of matrix A are combined to result in the B matrix. As indicated above, the specification does not describe how the position values of each sequence of matrix A is used to result in matrix B. Ms. Brouillet concludes paragraph 9 stating, "these rules are inherently clear to one of ordinary skill in the art by simply inspecting the values in matrix B". Paragraph 9 of the declaration fails to provide evidence to support the enablement for constructing Matrix B. In paragraph 10, Ms. Brouillet explains the construction of matrix C from matrix A. Similar to the explanation of the construction of matrix B, the explanation inserts conditional requirements that are not represented in the specification or claims and fails to indicate how all the values of matrix A are combined to construct matrix C. Ms. Brouillet's opinions, summarized in paragraph 11, that the disclosure and instant claims enable one to make the claimed invention are not sufficient to overcome the new grounds of rejection because the arguments are not supported by objective evidence.

NEW MATTER

The following rejection has been modified as necessitated by amendment.

Claims 1-10, 20, 28-29, and 31-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

Claims 1-10, 20, 28-29, and 31-32 recite the step of outputting identified motifs to a computer controlled display. The disclosure as originally filed is completely silent regarding any of the manners of output as recited in the outputting step of claim 1.

Claims 1-10, 20, 28-29, and 31-32 recite that **all** the steps of the method are performed on a programmed computer. The disclosure as originally filed is silent with regard to **all** the steps being performed on a programmed computer as instantly claimed.

Response to Arguments

Applicant's arguments filed 06 February 2009 have been fully considered but they are not persuasive. Applicant argues that claims 1-10, 20, and 28-29 do not contain new matter. The argument is not persuasive. First, applicant refers to the office action dated 06 August 2008. No office action of record exists that is dated 06 August 2008. The Office action dated 19 November 2008 explicitly

cautioned applicant against the introduction of new matter. Second, the paragraphs to which applicant points as evidence of support against the holding of new matter fail to recite or suggest limitations of a computer controlled display or that **all** steps of the method are performed on a programmed computer. Third, how the Office classifies an application is not germane to the holding of new matter. With respect to applicant's arguments regarding the use of the CLUSTALW program to generate the alignments of first step of the method, it is noted that the specification contains adequate support that a specifically programmed computer is employed to generate the alignments. It is brought to applicant's attention that the rejection of the claim as reciting new matter is not directed to the instantly recited limitations of the alignment step of the method in claims 1 or 32.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The following rejection is reiterated from the previous Office Action.

Claim 1, 2, 4, 5, 9-10 and 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rose et al. (Bioinformatics, Vol. 16, No. 4, p. 400-401, 2000) and in view of Zhang et al (New England Journal of Medicine, Vol. 340, No. 21, p. 1605-1613, 27 May 1999).

The claims are directed to a process for identifying motif in a set of sequences comprising aligning a set of sequences; comparing a reference sequence to the set of sequences; identifying a motif that mutated and outputting the identified motif. In an embodiment, a motif is a nucleotide and the sequences of the set are selected from a databank. In an embodiment the sequence is a wild type sequence. In an embodiment, the reference sequence is aligned to the

set of sequences. In an embodiment, the sequences are obtained from an organism having a high level of mutability.

Rose et al. shows a process of identifying sites of hyper mutability in HIV sequences. Rose et al. shows that a set of sequences is aligned and a reference sequence is compared to the set of sequences to identify the positions or motifs in the reference that have mutated (p. 401, col. 1). Rose et al. shows that mutated positions are identified and output (p. 401 col. 1). In an embodiment, Rose et al. show that the sequences comprise nucleotides (figure 1). In an embodiment, Rose et al. shows that the position of a motif in the reference sequence is the same position in the set of sequences (p. 401, col. 1). Rose et al. shows in figure 1 the comparison of 2 sequences from the same patient demonstrating hypermutability as compared to a reference sequence from the same patient, wherein the reference is interpreted to read on wild type. Rose et al. shows that an array or matrix is formed from the sequences to compare each nucleotide in the reference sequence. In an embodiment, Rose et al. shows the sequences are obtained from an organism having a high level of mutability (p. 400, col. 1). Rose et al. suggests that HIV sequences mutate during the course of antiviral therapy.

Rose et al. does not show that the identified mutations are correlated with known drug resistances or with catalytic site and/or in sites linked by noncompetitive inhibitors.

Zhang et al. shows that mutations occur in the course of treatment of patients with the drugs ritonavir, indinavir, saquinavir, zidovudine, and lamivudine

that target the reverse transcriptase and protease of HIV (p.1609, col. 1). Zhang et al. shows that by monitoring the appearance of mutation in a rapidly adapting organism for mutations that confer resistance to drug, effective drug treatment regimens may be developed that facilitate the decrease in the size of the pool of latent virus (p. 1612, col. 1-2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Rose et al. for identifying mutations in HIV sequences relative to a wild type reference with the correlations of mutation to drug resistances that arise in response to treatment of Zhang et al. because Zhang et al. suggest that it is advantageous to monitor the appearance of mutations in response to therapy and to modify treatment as a way to decrease the size of the pool of latent virus.

Response to Arguments

Applicant's arguments filed 10 February 2009 have been fully considered but they are not persuasive. Applicant argues the rejection based on the teachings of Rose and Zhang do not show the limitations of claim 6. The argument is not persuasive. As indicated in the rejection above, Rose and Zhang et al are cited for teaching the limitations of claims 1, 2, 4, 5, 9-10 and 28-29. Applicant argues that Rose et al. does not describe the limitation of identifying motifs not having mutated simultaneously or motif having mutated simultaneously at least once on at least one sequence of the set of sequences and not having mutated on another sequence of the set. This is not persuasive. Applicants clarification of the term "simultaneously" in the response filed 06 August 2008 at

page 10, lines 4-7, states, "Thus, in the context of the application, the terms "simultaneously" or "the same time" do not refer to the timing, of mutations in terms of chronological, geological or evolutionary time, but instead refer to whether such mutations are seen in the context of a particular matrix to occur together". In view of applicants argument regarding the term "simultaneously", the motifs or positions as identified by Rose et al. reads on the limitation of identifying motifs not having mutated simultaneously or motif having mutated simultaneously at least once on at least one sequence of the set of sequences and not having mutated on another sequence of the set (p. 401, col. 1). The rejection is maintained.

The following rejection is modified from the previous Office Action.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rose et al. in view of Zhang et al. as applied to claim 1, 2, 4, 5, 9-10 and 28-29 above, and further in view of Collins et al. (Chapter 13: molecular sequence comparisons and alignment *In* Nucleic acid and protein sequence analysis, IRL Press, ed. Bishop and Rawlings, p. 232-358, 1987).

Claim 3 is directed to an embodiment in which the motif is an amino acid.

Rose et al. in view of Zhang et al. shows a process of identifying sequence positions that mutate. Zhang et al. shows that an array of positions is created to produce a multiple alignment (p. 1607, col. 1). Rose et al. shows that a user selection is made to specify the positions of interest (p. 401, col. 1). Rose et

al. shows an embodiment in which positions that that mutate and the positions that do not mutate are determined.

Rose et al. in view of Zhang et al. does not explicitly show motifs are amino acids.

Collins et al. show that binary arrays can be formed to compare amino acid or nucleic acid sequences. Collins et al. call the array a dot plot (p.326). Collins shows that the dot plot is an array or matrix of j x i cells in which pair wise comparisons can be made ranging from 0-j to 0-i (p.326). Collins et al. shows the simplest type of dot plot consists of placing a dot in a cell in which the positions specifying the cell match (p. 326).

It would have been obvious to one of ordinary skill in the art to modify the method for identifying mutations of Rose et al. in view of Zhang et al. with the amino acid dot-plot comparison of Collins et al. because Collins et al. shows that the dot plot comparison is a simple technique for producing pair wise comparisons. It would have been further obvious to one of ordinary skill in the art at the time of invention to modify the method for identifying mutations of Rose et al. in view of Zhang et al. with the amino acid dot-plot comparison of Collins et al. because all the claimed elements were known, in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention. It would have been further obvious to one of ordinary skill in the art at the time of invention to modify the method for identifying mutations of Rose

et al. in view of Zhang et al. and the dot-plot of Collins et al. to highlight non-matches because the dot-plot technique was recognized as part of the ordinary capabilities of one skilled in the art. One of ordinary skill in the art would have been capable of applying this known technique to indicate non matches in sequences using the dot plot sequence comparison method that was ready for improvement and the results would have been predictable to one of ordinary skill in the art.

Response to Arguments

The rejection of claims 6-8 as unpatentable over Rose et al. in view of Zhang et al as applied to claims 1, 2, 4, 5, 9-10 and 28-29 and in further view of Collins et al. have been withdrawn and a new rejection made under 35 USC 112 First Paragraph. Although claims 6-8 were interpreted broadly with respect to the rejection over Rose et al. in view of Zhang et al as applied to claims 1, 2, 4, 5, 9-10 and 28-29 and in further view of Collins et al., applicant's arguments regarding the construction of Matrices B and C have been found persuasive to the extent that Rose et al. in view of Zhang et al as applied to claims 1, 2, 4, 5, 9-10 and 28-29 and in further view of Collins et al. do not show the steps as recited in claim 6 of the instant invention. Upon further consideration of the description of the construction of Matrices B and C as provided for in the instant claims and specification, a rejection under 35 USC 112 First Paragraph was required.

Applicant's arguments filed 10 February 2009 have been fully considered but they are not persuasive regarding claim 3. Applicant has not specifically

pointed out the deficiencies of the rejection in view of Collins et al as applied to claim 3. The rejection is maintained.

The following rejection is a new ground of rejection as necessitated by amendment of the claims.

Claims 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rose et al in view of Thompson et al (Nucleic Acids Research, Vol. 22, No. 22, p. 4673-4680, 1994).

Claim 32 is directed to a process for identifying motif in a set of sequences comprising aligning a set of sequences by a CLUSTAL algorithm; comparing a reference sequence to the set of sequences; identifying a motif that mutated and outputting the identified motif. Claim 33 is directed to the embodiment in which the CLUSTAL algorithm is the CLUSTAL W algorithm.

Rose et al. shows a process of identifying sites of hyper mutability in HIV sequences. Rose et al. shows that a set of sequences is aligned and a reference sequence is compared to the set of sequences to identify the positions or motifs in the reference that have mutated (p. 401, col. 1). Rose et al. shows that mutated positions are identified and output (p. 401 col. 1).

Rose et al doe not show the alignment is accomplished with a CLUSTAL algorithm.

Thompson shows multiple alignments can be generated using a CLUSTAL W algorithm (figure 1, and p. 4674, col. 2 to p. 4675, col. 2). Thompson et al. shows the CLUSTAL W algorithm for alignment has the benefit

of greatly improving sensitivity without sacrificing speed or efficiency shows (p. 4673, col. 1).

It would have been obvious to one of ordinary skill in the art at the time of invention modify the method of Rose et al for identifying hyper mutations in sequences with the method of generating alignments using CLUSTAL W of Thompson et al. because Thompson et al. shows the CLUSTAL W algorithm has the benefit of greatly improving alignment sensitivity without sacrificing speed or efficiency.

The following rejection is a new ground of rejection as necessitated by amendment of the claims.

Claims 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rose et al in view of Eddy (*Trends Guide to Bioinformatics*, 15-18, 1998, (preprint), [online] available at selab.janelia.org/publications.html).

Claim 32 is directed to a process for identifying motif in a set of sequences comprising aligning a set of sequences by a CLUSTAL algorithm; comparing a reference sequence to the set of sequences; identifying a motif that mutated and outputting the identified motif. Claim 33 is directed to the embodiment in which the CLUSTAL algorithm is the CLSUTAL W algorithm.

Rose et al. shows a process of identifying sites of hyper mutability in HIV sequences. Rose et al. shows that a set of sequences is aligned and a reference sequence is compared to the set of sequences to identify the positions or motifs

in the reference that have mutated (p. 401, col. 1). Rose et al. shows that mutated positions are identified and output (p. 401 col. 1).

Rose et al does not show the alignment is accomplished with a CLUSTAL algorithm or a Hidden Markov Model algorithm.

Eddy shows a method of generating sequence profiles using both a CLUSTAL algorithm and Hidden Markov Model (HMM) algorithm. Eddy shows a multiple sequence alignment is created using CLUSTAL W (p. 2). Eddy shows a profile is created from the multiple sequence alignment using a HMM algorithm (p. 2). Eddy shows profiles from HMM algorithms have the advantage of incorporating position specific scoring information derived from the frequency that a given residue (amino acid or nucleotide) is seen in an aligned column (p. 1).

It would have been obvious to one of ordinary skill in the art at the time of invention modify the method of Rose et al for identifying hyper mutations in sequences with the method of generating alignments and profiles of Eddy because Eddy shows profiles from HMM algorithms have the advantage of incorporating position specific scoring information derived from the frequency that a given residue (amino acid or nucleotide) is seen in an aligned column.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

The following provisional rejection is reiterated from the previous action.

Claims 1-10, 20, and 28-29 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-10, 21, and 29-30 of copending Application No. 11/480,014. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Response to Arguments

The provisional double patenting rejection will not be held in abeyance and is maintained from the previous action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone number is (571)272-9047. The examiner can normally be reached on 8:00am-5:00pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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29 April 2009

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